
Adeno-Associated Virus and Hematopoietic Stem Cells: The Potential of Adeno-Associated Virus Hematopoietic Stem Cells in Genetic Medicines.

Journal: Hum Gene Ther

Publication Year: 2020

Authors: Saswati Chatterjee, Venkatesh Sivanandam, Kamehameha Kai-Min, Jr Wong

PubMed link: 32253938

Funding Grants: Genome Editing of Sinusoidal Endothelial Stem Cells for Permanent Correction of Hemophilia A

Public Summary:

Scientific Abstract:

Adeno-associated virus (AAV)-based vectors have transformed into powerful elements of genetic medicine with proven therapeutic efficacy and a good safety profile. Over the years, efforts to transduce hematopoietic stem cells (HSCs) with AAV2 vectors have, however, been challenging. While there was evidence that AAV2 delivered vector genomes to primitive, quiescent, multipotential, self-renewing, in vivo engrafting HSCs, transgene expression was elusive. In this study, we review the evolution of AAV transduction of HSC, starting with AAV2 vectors leading to the isolation of a family of naturally occurring AAVs from human CD34(+) HSC, the AAVHSC. The stem cell-derived AAVHSCs have turned out to have remarkable potentials for genetic therapies well beyond the hematopoietic system. AAVHSCs have tropism for a wide variety of peripheral tissues, including the liver, muscle, and the retina. They cross the blood-brain barrier and transduce cells of the central nervous system. Preclinical gene therapy studies underway using AAVHSC vectors are discussed. We review the notable ability of AAVHSCs to mediate efficient, seamless homologous recombination in the absence of exogenous nuclease activity and discuss the therapeutic implications. We also discuss early results from an AAVHSC-based clinical gene therapy trial that is underway for the treatment of phenylketonuria. Thus, the stem cell-derived AAVHSC, offer a multifaceted platform for in vivo gene therapy and genome editing for the treatment of inherited diseases.

Source URL: <https://www.cirm.ca.gov/about-cirm/publications/adeno-associated-virus-and-hematopoietic-stem-cells-potential-adeno>